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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/760,046 | 01/12/2001 | Edith Mathiowitz | BU 111 | 1885 |
| 23579 | 7590 | 11/18/2004 | EXAMINER | |
| PATREA L. PABST PABST PATENT GROUP LLP 400 COLONY SQUARE SUITE 1200 ATLANTA, GA 30361 | | | SHEIKH, HUMERA N | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1615 | |
| DATE MAILED: 11/18/2004 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/760,046

Applicant(s)

MATHIOWITZ ET AL.

Examiner

Humera N. Sheikh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,6-13,15-23,25,26,34 and 35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,6-13,15-23,25,26,34 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 C.F.R. §1.114 filed 06/02/04, the Notice of Appeal and extension of time request (1 month-granted), both filed 04/08/04, the Amendment and Applicant's Arguments/Remarks filed 02/18/04 is acknowledged.

Claims 1, 3, 4, 6-13, 15-23, 25, 26, 34 and 35 are pending. Claims 1, 18, 21 and 23 have been amended. New claim 35 has been added. Claim 24 has been cancelled. Claims 1, 3, 4, 6-13, 15-23, 25, 26, 34 and 35 are rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 6-13, 15-23, 25, 26, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The preamble requires a dry, micronized particle to be produced, however, process step(e) does not result in a dry particle. Claim 3 is further confusing since no solid particles are produced. Clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 4, 6-13, 15-23, 25, 26, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah (WO 98/46212).

Shah teaches a method for making a composition comprising an active ingredient contained within polymeric microparticles, wherein a mixture of the active ingredient and the polymer are dispersed within a continuous phase, the resulting dispersion is frozen, and the water and organic solvents are removed from the dispersion by lyophilization (pg. 28, claim 1). The Shah reference also teaches spray drying, solvent evaporation, phase separation techniques and teaches that these processes are well known in the art as encapsulation methods (pg. 4, lines 17-20).

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Shah teaches a method of making polymeric microparticles containing a variety of active agents, such as protein drugs (Abstract). Shah does not teach the protein osteoprotegerin as recited in instant claim 10. One of ordinary skill in the art would desire to utilize any particular protein, based on the teachings of Shah, since Shah teaches that therapeutic results are obtained with proteins in general.

Shah does not teach the instant particle sizes and ranges of solvent to non-solvent, however, it is the position of the Examiner, that absent a demonstration of criticality, one of ordinary skill familiar with this art would be fully capable of determining suitable and effective particle sizes and ratios through the use of routine or manipulative experimentation to obtain the best possible results, as these are indeed variable parameters. Moreover, generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It would have been obvious to use the teachings of Shah, because Shah teaches similar, effective processes of forming microparticles containing active ingredients. One of ordinary skill in the art would have been motivated to use any well-known protein, and to manipulate particle sizes and ratios of the process components, depending on the desired end result. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant attempts to distinguish over the prior art of record, by incorporating process step (c) in the method. However, it is deemed obvious to encapsulate a macromolecular material in a solution. Encapsulation merely requires that the material be enclosed. Shah teaches encapsulation methods comprising spray drying, solvent evaporation, and phase separation techniques. Shah recognizes, for example, emulsions of polymers and active ingredient that can be atomized into frozen nonsolvent overlaid with liquefied gas to form particles (pg. 4, lines 17-23). The distinction appears to be based on the order of the particular process steps, however, it is held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (See *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). Additionally, the selection of any order of mixing ingredients is *prima facie* obvious (See *In re Gibson*, 39 F.2d 975, 5USPQ 230 (CCPA 1930). Therefore, the prior art teaches similar processes of forming microparticles containing active ingredients and renders the instant invention *prima facie* obvious.

Response to Arguments

Applicant's arguments filed 06/02/04 have been fully considered but they are not persuasive.

Firstly, Applicant argued regarding the 35 U.S.C. §102(b) rejection of claims 1, 3, 7-9, 11-13, 15-17, 19 and 23-26 stating, "Claim 1 requires forming an emulsion containing (i) a macromolecular material, (ii) an organic solvent, and (iii) a protein, peptide or drug agent (steps

1 and 2) and then freezing this emulsion (step 3). Thus, the emulsion formed in step 2 is not a double emulsion. In contrast, Shah does not disclose forming a single emulsion and freezing the emulsion, as required by Claim 1.”

This argument has been fully considered. The 35 U.S.C. §102(b) rejection has no longer been applied in this Office Action by virtue of the Amendment. However, the instant pending claims have now been rejected under 35 U.S.C. §103(a). The argument that Shah discloses a double emulsion, whereas the instant claims do not is not persuasive since, the instant claims utilize ‘comprising’ claim language and thus do not exclude the double emulsion, which is a species of emulsion formulations. Shah teaches a similar process resulting in the same end product as that presently claimed.

Secondly, Applicant argued, “Shah does not disclose the final step required by Claim 1. Following lyophilization (step 4), the macromolecular material is dissolved in a solvent that is a non-solvent for the agent. Shah does not describe an additional step of dissolving the encapsulating materials. Thus, Shah does not disclose every element of claim 1 and its dependent claims.”

This argument has been considered and was found persuasive in terms of the 102(b) anticipation rejection. Accordingly, the 102(b) rejection has been withdrawn. The claims, as now rejected, stand obvious under §103(a) based on the teachings of Shah. Shah teaches effective methods of forming microparticles containing active ingredients, using various techniques, such as spray drying, solvent evaporation and phase separation techniques, which are all well known encapsulation methods. Applicant’s specification is also directed to microencapsulation techniques. The prior art desires and suggests a similar process and end

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product as instantly claimed. The difference appears to be an additional step to achieve the same end product. In the case that the difference is the order of the particular process steps, it is held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (See *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). Additionally, the selection of any order of mixing ingredients is *prima facie* obvious (See *In re Gibson*, 39 F.2d 975, 5USPQ 230 (CCPA 1930). It is the Examiner's position that the prior art teaches a similar composition in the same field of endeavor as the Applicant to obtain the same results. Thus, no significant *patentable* distinction has been observed between the instant invention and the prior art.

Lastly, Applicant argued regarding the 35 U.S.C. §103(a) rejection of claims 1, 3, 4, 6-13, 15-26 and 34 over Shah stating, "Shah discloses a process for encapsulating proteins. This process involves different steps than the claimed method. There is no suggestion to modify its process so that it can form a single emulsion which is frozen. Additionally, there is no suggestion to modify its methods to include a dissolution step following the lyophilization step. Such a step would remove the polymer that encapsulates the active agent; and thereby defeat the purpose of Shah's encapsulation process."

These arguments have been fully considered, but were not persuasive. The instant claims permit the inclusion of additional steps besides those recited, based on the instant 'comprising' claim language. Shah teaches a method for making a composition comprising an active ingredient contained within polymeric microparticles, wherein a mixture of the active ingredient and the polymer are dispersed within a continuous phase, the resulting dispersion is frozen, and the water and organic solvents are removed from the dispersion by lyophilization

(pg. 28, claim 1). The argument that 'Shah does not include a dissolution step following lyophilization' is not persuasive since similar processes of encapsulation are clearly suggested by the prior art. Moreover, the additional process step (e) is unclear in the sense that the instant method recites a 'method for making *dry* micronized particles' and the additional dissolution step following lyophilization in step (e) would not result in a dry particle. The prior art recognizes the making of polymeric microparticles containing active ingredients using well-known, effective techniques of the art. No unexpected or unusual results are observed using Applicant's claimed method. Hence, the instant invention remains obvious and unpatentable over the prior art of record.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh *H.N.S.*

Patent Examiner

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November 03, 2004

Thurman K. Page
THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600